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LETTER TO THE EDITOR

Bone remodeling effect of cyclosporine protects against steroid-induced osteopenia

Delayed reply from authors

We thank Goffin et al for pointing out additional confounding factors that might account for differences in bone mineral density (BMD) changes as reported in our article published by *Kidney International* [1]. Since all our premenopausal women had normal menstruations prior to transplantation, a change in their estrogen status can be eliminated. With regard to the physical fitness of all our patients (who received transplants within a year after starting dialysis), their physical status was as good after transplantation as before. Statins and thiazides, which may increase BMD and reduce the risk of fractures [2], was prescribed in none of our patients. Although the hypercalciuric furosemide was prescribed more frequently in those whose BMD decreased (60 versus 30%), its role in the decrease of BMD in this group is unlikely because the parathyroid hormone (PTH) levels were comparable in the two groups of patients. Therefore, in our opinion, we can reasonably eliminate these factors as being confounding. Only the higher dose ratio of cyclosporine on prednisone was associated with improvement of the lumbar Z score.

The significant BMD decrease observed in the patients described by Goffin et al is not in contradiction with our observations because of differences in patient selection, techniques used for BMD measurement, and period of observation. First, our population was highly selected to eliminate confounding factors. Since none of our patients had had rejection, the cumulative dose of a steroid was certainly lower than that of Goffin et al.

Second, the beneficial effect of cyclosporine on BMD was indirectly demonstrated only because of the increase of lumbar Z score measured by quantitative computed tomography (QCT). This method is more sensitive than double-energy x-ray absorptiometry (DEXA) to detect changes in the trabecular bone. Indeed, metabolically active surfaces of trabecular bone are much larger for a given volume than those of cortical bone. Furthermore, QCT measures an actual volumetric density of vertebrae trabecular bone compared to DEXA, which measures an areal projection of bone mineral content of both trabecular bone and two layers of cortical bone.

Finally, our period of observation was 3 to 24 months while that of Goffin et al was 1 to 12 months post-transplantation. It is well documented that in non-selected patients lumbar bone loss is predominant during the first 6 months (−6.8%), whereas further bone loss between 6 and 18 months is only 2% [3]. It is remarkable that Grotz et al [4], who still found 1% loss during the second year, found an increase in DEXA BMD when sequential measurements at 12-month intervals were done 3 to 20 years after transplantation while prednisone dose was decreased to a similar level as in our patients (0.12 mg/kg/day) and cyclosporine dose was 3.4 to 3.8 mg/kg/day, a little lower than in our patients (about 5 mg/kg/day).

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